

Exhibit B

**UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON**

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION THIS DOCUMENT RELATES TO WAVE 1 CASES	Master File No. 2:12-MD-02327 JOSEPH R. GOODWIN U.S. DISTRICT JUDGE
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RULE 26 EXPERT REPORT OF MICHAEL THOMAS MARGOLIS, M.D.

I. BACKGROUND AND QUALIFICATIONS

My curriculum vitae, attached hereto as Exhibit "A", more fully reflects my training, background, and publications, including those for the past ten years. I graduated from the University of Kansas Medical School in Kansas City, Kansas in 1987. I am licensed to practice medicine in the states of Wisconsin and California, where I also hold a valid California fluoroscopy x-ray supervisor and operator certificate. I did my internship in internal medicine for one year followed by three years of obstetrics and gynecology residency training under the direction of the father of urinary incontinence surgery, Dr. Kermit E Krantz, M.D. (co-founder of the MMK procedure which is predecessor to the Burch procedure(still considered the gold standard procedure for the treatment of urinary incontinence)). After completing my residency, I became one of only a handful of fellowship-trained pelvic surgeons in the country to complete the pelvic surgery fellowship at Emory University in Atlanta, Georgia where I trained under the World-renowned Johns Hopkins surgeon, Dr. Clifford Wheelless.

I currently hold hospital privileges at Mills Peninsula Medical Center in Burlingame, California, Good Samaritan Hospital in San Jose, ValleyCare Hospital in Pleasanton, Seton Medical Center in Daly City, Sequoia Hospital in Redwood City, El Camino Hospital, O'Connor Hospital in San Jose, Community Hospital of the Monterey Peninsula in Monterey, and several surgery centers. I currently serve as Vice Chairman in the Department of Obstetrics and Gynecology at Peninsula Hospital in Burlingame, California.

I am Board Certified in Obstetrics and Gynecology by the American Board of Obstetrics and Gynecology. I recently took and passed the first subspecialty board certification exam in the subspecialty of Female Pelvic Medicine and Reconstructive Surgery, thus becoming a member of the first class of Board-Certified Pelvic Surgeons in the country. I am a fellow in good standing of the American College of Obstetrics and Gynecology and the American College of Surgeons and I am a member of multiple societies including: the American Urogynecologic Society, the Society of Pelvic Reconstructive Surgeons, the Northern California Chapter of the American College of Surgeons and the Kermit E. Krantz Society.

I am District VII delegate to the California Medical Association. I have served at various hospitals as member of various medical executive committees including service as chairman of the OB/GYN department at Los Gatos Community Hospital, quality management committees at Northwestern University Hospital, Stanford Hospital, Peninsula Hospital and several hospitals in Wisconsin. I have served as president of the Peninsula Gynecologic Society and the Shufelt Gynecologic Society in San Jose, California.

I have held faculty positions in the Department of Obstetrics and Gynecology at Emory University in Atlanta Georgia, Northwestern University in Chicago, Illinois, and Stanford University in California, where I also served as chief of the division of gynecology and founder

and director of The Stanford Center for Pelvic Reconstructive Surgery and Urogynecology. I have held clinical faculty appointments in the Department of Obstetrics and Gynecology at Stanford University and the University of Wisconsin in Milwaukee where I received the teaching excellence award in 2009.

I have been and continue to be actively engaged in the education and training of medical students, resident physicians, fellows and faculty at numerous universities and I currently teach on a daily basis and hold a clinical faculty position in the Department of Obstetrics and Gynecology at the David Geffen School of Medicine at UCLA, the Department of Obstetrics and Gynecology at Mbarara University in Uganda (where I also hold the title of visiting lecturer), and I am currently gynecology rotation site director at Valley Medical Center., Department of Obstetrics and Gynecology residency program in San Jose, California. I have performed animal testing on many novel surgical instruments and I have performed field testing in humans for Boston Scientific sling anchor instruments in the past.

I have published numerous peer-reviewed and non-peer-reviewed publications in the field of obstetrics and gynecology and have written several books chapters in the field as well. These publications including those in the past 10 years are listed in my C.V. (Exhibit A). I have lectured extensively throughout the US and abroad on numerous subjects involving sling and mesh complications and advanced pelvic surgery, including the treatment of prolapse and incontinence. I have presented original scientific peer reviewed articles at the Society of Gynecologic Surgeons and I have presented surgical videos at the American College of Obstetricians and Gynecologists annual meeting. I have served as reviewer for the Journal of Reproductive Medicine and the International Journal of Obstetrics and Gynecology.

Pursuant to a request by the FDA, on September 8, 2011, I testified at the FDA hearing for the Obstetrics and Gynecology Devices Panel in Gaithersburg, Maryland on the serious issue of complications of transvaginal synthetic mesh placement. My address was based on my knowledge, experience, education, and training as a pelvic surgeon and on observations made during scores of salvage operations I have performed on women who have experienced mesh and sling complications since 1996. During my address, I made the analogy that extirpation of vaginal mesh was akin to using a hammer and chisel and trying to remove the rebar from a sidewalk while leaving the cement otherwise intact and not damaging the water mains and power lines below. Since my FDA testimony and based upon my further experience with slings and mesh, I have found that it may even be more dramatic and challenging than that.

I am medical director of Medlend Medical Missions to Developing Countries, a nonprofit organization that provides free surgical care to women in need around the globe. I have participated in IO different surgical missions throughout Ghana, Peru, and Uganda. I am team leader of the yearly fistula mission to Uganda where I direct trainees from around the world in the repair of complex gynecologic injuries, often related to pelvic organ prolapse and incontinence.

I am in private practice of Pelvic Surgery and Urogynecology in the Bay Area of California. I perform on average 10 major surgical procedures per week. I have performed over 25,000 surgical procedures in my professional career, including approximately 1,500 organic (non-synthetic) sling procedures. The majority (90%) of my patients are referred to me by other gynecologists for complications associated with prior gynecologic surgery, prolapse, incontinence, fistulas and polypropylene or other synthetic mesh and sling related injuries. Since 1996, I have removed over 300 mesh or sling systems in patients who have suffered numerous

complications. Although when removing mesh, I do not always know what particular mesh was implanted. In the early years, as my expertise at explant surgery developed, in order to assist in the removal, I would gain access to the implant records and to learn which particular synthetic mesh was involved. In this regard, I would also review the applicable Instructions for Use (IFU). Frequently, the product has been one of the TVT products manufactured by J&J/Ethicon, including the product at issue in this case.

Within the last 1 to 2 years, the number of patients with synthetic mesh or sling related complications presenting to me for definitive surgical treatment has increased dramatically. I now remove on average two sling or mesh systems per week and the number continues to rise. Patients are referred to me for sling and mesh complications from across the country. These patients include women with the TVT retropubic device.

In order to more fully understand how to deal with the complications of these synthetic mesh systems and to remove them as effectively as possible, I have personally observed numerous sling and mesh insertion procedures by colleagues of mine and through industry videos from a variety of manufacturers, including J&J/Ethicon for their TVT products. As well, I have studied textbooks, publications, IFU's (including those from J&J/Ethicon for the TVTs), surgical videos, cadaver dissections and countless operative reports as part of my study of sling and mesh surgeries. I have conferred with colleagues at conferences and in person throughout the country and abroad on synthetic mesh related complications.

Based on this education and experience, I am uniquely qualified and experienced as an expert in synthetic sling and mesh related issues and complications and can provide absolute standard of care testimony on all clinical aspects of this subject matter.

II. OVERVIEW OF INCONTINENCE AND TREATMENT HISTORY

The average age of menopause in US women is 50 years and the life expectancy is 80 years. Thus, women live more than one third of their lives in the postmenopausal years. US Census data from 2006 show that of the 300 million US citizens one half were women 16 million of whom were women age of 45 and older. Between 1995 and 2020, the Census Bureau predicts an increase in the number of women 45 years old and over of more than 25 million. Since the majority of incontinence and prolapse occurs in the late and post-reproductive age group pelvic floor defects and incontinence will continue to affect a large number of women now and well into the future. This population provides an attractive target for marketing campaigns by device manufacturers seeking to capture a high market share for devices used in the treatment of these conditions.¹

Almost 200 procedures have been described in the literature for the treatment of stress incontinence alone. These procedures can be broken down into seven major categories including:

1. Anterior repair
2. Needle suspension procedures
3. Retropubic urethropexy - Open vs. scope
4. Sling operations - Traditional vs. new
5. Perry urethral injections
6. Artificial sphincter
7. Urinary diversion

The first sling procedure for SUI was described in 1907. This procedure, later called the Goebell-Frankenheimer-Stoeckel procedure utilized the patient's own ligaments to support the return. Its only indication was for type III stress incontinence which is also known as intrinsic sphincter deficiency (ISD). ISD is characterized by an absence of urethral hypermobility, low urethral pressures and is typically seen in patients with a history of previous urethral surgery. By

¹ Wall, The Perils of Commercially Driven Surgical Innovation, Am J. of Obstetrics and Gyne Jan 2010; 202:30e1-4.

definition, synthetic slings are obstructive procedures which are always done blindly, thus increasing the risk of injury to adjacent organs.

In 1998, Ethicon's TVT Retropubic device ("TVT") was cleared for marketing. TVT is a suburethral sling used for the treatment of female stress urinary incontinence (SUI). The TVT kit includes the actual TVT device, which is a polypropylene mesh sling attached to needles, and surgical tools for implanting the sling. The TVT sling itself is made from Prolene® polypropylene mesh, which is constructed of knitted filaments of extruded polypropylene strands.

III. COMPLICATIONS ASSOCIATED WITH THE TVT

In my opinion from my professional experience and research, there are a number of serious and often permanent complications associated with implanting a polypropylene synthetic mesh like the TVT to treat incontinence. I have reached these opinions based on my personal experience explanting meshes, through my personal research, through my review of Ethicon's internal documents, and my review of the depositions and experts reports that have been provided to me. Unfortunately, it is now well known that the use of polypropylene mesh slings like the TVT are associated with serious and often permanent complications. These complications can include:

1. Development of abnormal tissue between the posterior urethra and the anterior vaginal wall;
2. Thickening and disfigurement of the vaginal wall;
3. Scar plate formation;
4. Distal urethral narrowing;
5. Temporary and permanent foreign body giant cell reaction;
6. Temporary and permanent chronic, debilitating pelvic pain;
7. Temporary and permanent dyspareunia;
8. Urinary problems, including: Urethral injury, Voiding dysfunction, De novo detrusor instability or urgency, Urinary retention/obstruction, Urinary retention (temporary or permanent), Urinary tract infection, Dysuria, Hematuria, and Worsening or recurrence of incontinence;

9. Erosions, including into surrounding tissue and organs, that can recur and require numerous surgeries;
10. Perforation of the surrounding organs;
11. Injury to partner during intercourse;
12. Serious and chronic inflammation, that is not slight or transient;
13. Chronic foreign body response;
14. Permanent nerve injury;
15. Defecatory problems, including chronic debilitating pain;
16. Mesh degradation;
17. Cytotoxic;
18. Toxic shock syndrome;
19. Difficulty treating infections, including de novo urinary tract infections that do not resolve with aggressive treatment or removal of the mesh;
20. Vaginal scarring which is greater than disclosed in its IFU;
21. Sarcomas at the site of implantation.

When these complications arise, which they frequently do, additional surgery may be needed. A revision surgery can be as simple as cutting extruded mesh or much more invasive such as an explant surgery. Each of these additional carries additional risks for the patient, especially due to the scarring that has resulted from the initial implant procedure. As a result of the implantation and subsequent removal of a TVT sling, a patient can be injured in many ways, including the need for additional surgeries, increased scarring, damage and deformity to her vagina, voiding symptoms, and recurrence of her SUI or de novo incontinence.

Synthetic sling and mesh procedures expose patients to triple the surgical risk of non-mesh repairs. Compared to a repair surgery that does not use a synthetic mesh, when complications arise, the patient with a synthetic sling implant has to then undergo another risky surgery to remove the mesh.

Revision surgeries further complicate a bad situation. Even if the mesh is completely removed, which is difficult, the patient then still suffers from the original problem of incontinence but with the addition of a damaged and scarred pelvic region. For subsequent surgery under these circumstances, a surgeon faces an operative field that is damaged, thus increasing the risk of complications and a higher failure rate of repair. In his textbook,

Reoperative Gynecologic Surgery, 1991, David Nichols states the obvious, “It is important that every effort be made to ensure the success of the first operative procedure undertaken as treatment of SUI. This is especially true since it is the first operative procedure that is most likely to cure a patient's SUI. Subsequent procedures have failure rates that increase in proportion to their number.”

Scar tissue is a permanent condition and will probably be problematic for the rest of the patient's life. A patient who has undergone an implant surgery and then subsequent revision surgery due to complications from the implant will likely suffer from a permanently disfigured vagina with permanently diminished function. For the patient, this translates into never regaining function of her vagina, never being completely pain free during intercourse, and never being completely free of pelvic pain.

These risks are well known now. Numerous Ethicon employees have testified that they were aware of the risks discussed above, including Ethicon Medical Directors Dr. Piel Hinoul, Dr. David Robinson, Dr. Martin Weisberg, and Axel Arnaud.² Even at the time the TVT was launched, internal documents reflect that all of the risks associated with implanting a synthetic mesh such as the TVT were known. In fact, Ethicon updated the warnings in the TVT Instructions for Use in 2015 to include many of these risks.

IV. CAUSES OF THE COMPLICATIONS

In my opinion from my professional experience and research, the above adverse events are caused by one or a combination of defects in the mesh or techniques associated with the use of Ethicon's TVT as described below. I have reached these opinions based on my personal experience explanting meshes, through my personal research, through my review of Ethicon's

² (Robinson (July 25, 2013) 448:4 - 451:12, (September II, 2013) 28:1-288:20; 293:21-293: 11 298; 18-24, 305:20-306:2, 306:7-23;329: 12-331:20, 1136:23 - 1140: 17; Hinoul (June 27, 2013) 547:11 - 557:7; Weisberg (August 9, 2013) 930: 3-8, 951:6-10, 951:11-16; 944; 16-945:5; 947:4-19; 968:12-972:21, Arnaud (July, 19, 2000) 66:8 to 66:19, 114:21 to 127:11); ETH.MESH .06372356 - ETH.MESH .06372363.

internal documents, and my review of the depositions and experts reports that have been provided to me.

A. The TVT Causes a Chronic Foreign Body Response

Mesh, when implanted into the vagina, is a foreign body. It is the human body's natural response to react to the presence of the mesh. A foreign body response is characterized by inflammation, soreness and pain at the site of the foreign body – here, the implanted mesh. The Ethicon Instructions for Use (“IFU”) recognize that this reaction is likely to occur. The IFU, however, described this response as “transient.”³ This is not consistent with what I have seen in my professional experience, nor with Ethicon's own internal documents.⁴

I have treated a number of women who have suffered from chronic long-term foreign body response to implanted mesh. These women often present with severe inflammation at the site of the implant that is persistent and painful. This inflammatory response can, in turn, lead to deformation of the mesh and damage to the tissues surrounding the mesh. Severe inflammation also leads to shrinkage and contraction of the mesh and the surrounding tissues and erosion.⁵

Severe inflammation can also lead to degradation of the mesh itself.⁶ Ethicon's scientists have demonstrated in animal studies that the mesh used in the TVT products degrades for years after implantation.⁷ Degradation of Ethicon's mesh has been well described in a number of

³ Until 2010, the IFU stated that the mesh was: “non-reactive with a minimal and transient foreign body reaction.” In 2010, Ethicon removed the word “transient.”

⁴ ETH.MESH.00211259 (“the foreign body reaction is not transitory – it doesn't ever go away, but decreases over time to a minimal level.”).

⁵ See, e.g., Vailhe Dep. (6/21/13) 383:8-19; Klinge, U., et al., *Shrinking of Polypropylene Mesh In Vivo: An Experimental Study in Dogs*, Eur J Surg 1998, 164: 965-969; Klinge, U., *Foreign Body reaction to Meshes Used for the Repair of Abdominal Wall Hernias*, Eur J Surg 1998, 164:951–960. Note that I refer to documents and scientific articles concerning hernia meshes because it is my understanding from Ethicon's internal documents that the mesh used in the TVT devices is the same as that used in Ethicon's early hernia meshes. See Smith Dep. (2/3/2014) 723:9-724:6 (“The first generation (old, old) mesh is utilized currently in the TVT product....”); ETH.MESH.10633520 at 3522.

⁶ Burkley Dep. (5/22/13) 184:17-24 (admitting that severe inflammation can lead to degradation of the mesh, shrinkage and contraction).

⁷ Burkley Dep. (5/23/13) 315:8-13 (discussing tests of mesh in dogs).

scientific articles, internal and external Ethicon studies.⁸ Degradation can also occur from the natural ecosystem in the vagina, including hydrogen peroxide and other compounds that can degrade polypropylene.⁹ However, the TVT IFU states, incorrectly, that the mesh is inert and not subject to degradation.¹⁰ In my opinion, this statement is false and misleading to physicians and patients.

This, unfortunately, establishes a vicious cycle of inflammatory foreign body response leading to mesh degradation leading to enhanced inflammatory foreign body response, etc. In the end, these women present with chronic pain, difficulty urinating, painful sexual encounters, tissue degradation, erosions, recurrent and difficult to eradicate infections and loss of sexual motivation or desire. Many of these problems are chronic and do not subside with removal of the mesh and often lead to the need for additional surgeries all of which increases the risk of and can lead to permanent damage to the urinary sphincter, worsening or de novo incontinence, scarring and chronic, debilitating pain.

It is my opinion that the Prolene mesh used in Ethicon's TVT products is not suitable for implantation in the vagina. Despite developing newer, safer polypropylene meshes that had larger pores and were lighter weight, Ethicon continued to use the old construction Prolene mesh which is associated with a number of problems as discussed in this report. Ethicon's TVT mesh products cause chronic foreign body responses and severe inflammation; a response Ethicon

⁸ ETH.MESH.02589032 and ETH.MESH.07192929 (May 18, 2011) (PA Consulting Report: Investigating Mesh Erosion in Pelvic Floor Repair and PowerPoint presentation stating: "[p]olypropylene can suffer from degradation following implant... a process which initiates after a few days post implantation in animal studies."; Clave, A., *Polypropylene as a Reinforcement in Pelvic Surgery is Not Inert: Comparative Analysis of 100 Explants*, I Urogynecol J 2010 21:261-270; Costello C., et al., "Characterization of Heavyweight and Lightweight Polypropylene Prosthetic Mesh Explants from a Single Patient," Surgical Innovation, 2007, 143:168- 176).

⁹ Sunoco MSDS; see also EB-405, *The Durability of Polypropylene Geotextiles for Waste Containment Application* (2011) ("[P]olypropylene is vulnerable to the following substances: highly oxidized substances such as (peroxide), certain chlorinated hydrocarbons (halogenated hydrocarbons), and certain aromatic hydrocarbons.").

¹⁰ ETH.MESH.02340406 (TVT IFU (May 2015) claiming mesh "is not absorbed, nor is it subject to degradation or weakening by the action of enzymes.").

falsely described as “transient” in its TVT IFUs. Ethicon’s TVT mesh degrades in the vagina which in turn leads to enhanced foreign body response and more inflammation. The increased inflammation further increases the degradation of the mesh – and the vicious cycle continues.

As a treating physician it would be important for me to know that Ethicon’s mesh could degrade in the vagina and that it would produce a severe inflammatory response. This information would inform my treating decision when recommending treatment to a woman suffering from SUI. In addition, it would inform my treatment of a woman experiencing the adverse effects described above. Physicians expect and rely upon a medical device manufacturer to truthfully report the known qualities and risks of its products, and Ethicon failed to do so. Ethicon’s TVT products are not suitable for their intended use to treat SUI.

B. The TVT Causes Fibrotic Bridging & Scar Plate Formation

The pore size of the mesh used in Ethicon’s TVT devices is best described as “heavy weight, small-pore.”¹¹ Small pore mesh has been demonstrated to increase fibrotic bridging which in turn leads to increased scar plate formation, contracture, shrinkage and effectively a stiffer mesh.¹² The fibrotic bridging and scar plate prevents tissue in-growth and causes complications, including, among other things, pain with the rigid mesh, shrinkage or contraction of the mesh, erosions due to mechanical irritation in the tissue of a rigid, nerve entrapment, chronic pain, recurrence, de novo or worsening incontinence, dyspareunia, wound infection, defecatory dysfunction, vaginal scarring, wound healing problems, abscess formation, and the need for additional surgeries.

¹¹ ETH.MESH.05918776; Batke Depo. (Aug. 1, 2013) at 87:12 - 88:10, 113:3 - 114:3, 257:23 - 259:13; Holste Depo. (July 29, 2013) at 51:3 - 53:6, 55:22-57:4; Vailhe Depo (June 20, 2013) at 182:2 185:5.

¹² See, e.g., B. Todd Heniford 2007 “The benefits of lightweight meshes in Ventral Hernia Repair in Ventral Hernia Repair” Video produced by Ethicon.

Ethicon's documents admit that curling/roping, frayed edges and inadequate pore size of mesh can lead to the harms of erosion, recurrence, and pain.¹³ Former Medical Director, David Robinson, testified that the pore size of mesh "[c]ould reduce, the tissue might not encapsulate . . . the tissue might not grow through the mesh. It can become encapsulated and then it could cause . . . a rejection of the mesh" which could lead to erosion.¹⁴ In fact, Ethicon developed lighter weight, large pore meshes in order to minimize the complications seen with heavyweight meshes like the Prolene used in TVT.¹⁵

I personally have explanted meshes that have exhibited the characteristics described in these videos, e-mails and studies. I have treated these women for the very complications listed above – all of which were discussed extensively in Ethicon internal e-mails and studies.

Based on my experience, review of the scientific literature and Ethicon's internal documents, it is my opinion that the Prolene mesh used in the TVT is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women. In addition, Ethicon failed to inform physicians and patients that its mesh was susceptible to fibrotic bridging which could lead to painful erosions, infections, nerve injury, dyspareunia, the need for multiple surgeries, chronic inflammation and pain among other complications.

This information is important for the treating physician who is attempting to have an informed conversation about the risks and benefits of various treatments for her SUI. In addition, it is critical information for the physician who is treating a woman who presents with these complications. Just as important, and as discussed in more detail below, Ethicon does not provide a treating physician with any guidance regarding how to treat a woman who is experiencing a mesh that has effectively become one large scar-plate. In sum, Ethicon failed to

¹³ ETH.MESH.01218019.

¹⁴ Robinson 9/11/13 1070:23-1072:25.

¹⁵ Holste 7/29/13 51:3-53:6.

inform physicians about these risks associated with fibrotic bridging (as a result of small-pore mesh), which means a physician could not properly discuss these risks with his or her patients, and Ethicon failed to provide any guidance or training on how to treat a patient who presented with fibrotic bridging or scar-plate formation. In my experience and my review of other IFUs, physicians expect and rely upon the manufacturer to provide this information as the manufacturer designed the device and has the most experience available to it to properly report on the risks with the device.

C. The TVT Causes Infections and Greatly Enhances the Probability of Experiencing Serious, Resistant Infections

As noted above, the TVT mesh is the same mesh as that originally used in the hernia application. However, one of the major differences between the use of mesh for hernia repair versus in the vagina is the nature of the surgical field. When placing a transvaginal mesh, the device is necessarily being placed in a contaminated surgical field. This alone can lead to severe debilitating infections, chronic foreign body response, severe inflammation, pain, painful sex, erosions, and the need for additional surgeries.¹⁶

However, the probability of severe infection is further increased due to the nature of the mesh itself. That is, the weave of the mesh effectively creates perfect, protected sites for bacteria to colonize. In addition, the microscopic flaws and degradation of the mesh fibers themselves provide fertile areas for bacterial growth. As discussed below, when mesh is implanted it can fray and deform creating additional surfaces ripe for bacterial colonization. These bacteria can secrete an encasing biofilm which shields the bacteria from destruction by the body's natural defenses.¹⁷

¹⁶ Shah, K, et al., Bacteriological Analysis of Explanted Transvaginal Meshes (Abstract 1144); ETH.MESH. 00006636.

¹⁷ Osterberg, B., et al., *Effect of Suture Materials on Bacterial Survival in Infected Wounds: An Experimental Study*, Acta. Chir. Scand 1979, 145:7 431-434; Merritt, K., *Factors Influencing Bacterial Adherence to Biomaterials*, J

Hence, implantation of the mesh in a contaminated field can lead to infection and an inflammatory chronic foreign body response. These effects are enhanced by the very nature of the mesh itself – the microscopic defects in the fibers, the frayed and deformed mesh, the weave of the mesh (particularly if the mesh is small-pored as is the TVT mesh). These design defects create fertile ground for bacterial colonization and severe infection and inflammation. The mesh also allows the bacteria to shield itself from the body's immune response by providing protected pockets for colonization of the bacteria, thus, creating a biofilm.

In its IFU, Ethicon states that the mesh may “potentiate infection.” As a treating physician, this statement is misleading. In fact, the very use of the device itself in a contaminated field likely will *cause* infection – not merely potentiate an already existing infection. This infection likely will be further exacerbated by the design of the mesh – the inherent microscopic defects in the fibers, the weave of the mesh (small pores), the defects of fraying and mesh deformation and the creation of biofilm in the pockets created by the mesh. Mesh-induced infections can be very difficult to eradicate and lead to chronic pain and inflammation, erosion (spreading the infection to other surrounding areas),¹⁸ dyspareunia, the need for removal of the mesh (in one or multiple surgeries), tissue damage and death, urinary pain and dysfunction and de novo incontinence.

Ethicon failed to properly inform physicians and patients of the risk of infection caused by the TVT procedure particularly when combined with the design of the mesh itself. I have personally seen the terrible outcomes associated with these severe infections, including the

Biomat Appl 1991, 5:185-203; An, Y., *Concise Review of Mechanisms of Bacterial Adhesion to Biomaterial Surfaces*, J Biomed Mater Res (Appl Biomater) 1998, 43:338-348; The TVM Group: J. Berrocal, et al., *Conceptual advances in the surgical management of genital prolapsed*, J Gynecol Obstet Biol Reprod 2004, 33:577-587.

¹⁸ ETH.MESH.02089392 (“Consensus: Erosion is a risk. Erosion, possibly an infection response. Typically seen by 3 mos, usually by 6-12 mos. Can present late, 3 years. To vagina-not a good situation. To bladder, urethra or rectum-a very bad situation.”).

chronic foreign body response that persists even when the mesh is explanted, severe inflammation, persistent, chronic pain, painful intercourse, erosions and repeated erosions, persistent infections that are difficult to fully eradicate, urinary tract infections, pain during urination and the need for multiple surgeries to achieve mesh removal.¹⁹

D. Problems Attributable to Ethicon's Cutting Processes.

Ethicon cuts its TVT mesh to size by one of two methods: by machine (mechanically-cut) or with a laser (laser-cut). The method by which mesh is cut significantly impacts how that mesh will perform during the implantation surgery and while implanted in a woman's body.²⁰ Despite these significant differences, Ethicon chose to inform physicians that there was no real difference in performance between the meshes.²¹ This was misleading.

1. Mechanically Cut Mesh

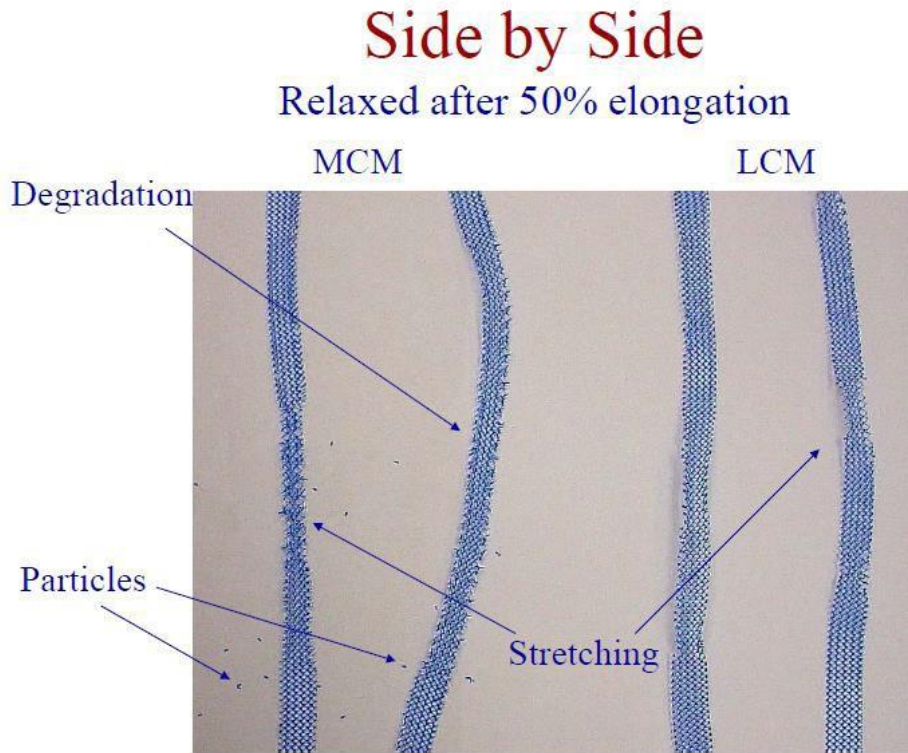
When it is cut to size by mechanical means, the edges of the mesh are sharp and have a tendency to cut into the surrounding tissue. In a presentation by Ethicon's engineer, Gene Kammerer, significant degradation in the form of fraying of the cut edges of the of the mesh and a loss of some of the edge particles was observed in the mechanically-cut mesh (MCM) after it had been elongated by 50%, while the TVT mesh that was laser-cut (LCM) demonstrated less particle loss, fraying and degradation.²²

¹⁹ The PROLENE IFU by comparison states as follows: "PROLENE Mesh in contaminated wounds should be used with the understanding that subsequent infection may require removal of the material." ETH.MESH.02342102.

²⁰ ETH.MESH.00687819; Depo. Robinson (July 25, 2013) 585:12-23.

²¹ ETH.MESH .00858252.

²² ETH.MESH.08334245.



In addition to fraying and resultant particle loss, the mechanically-cut TVT mesh also tends to more drastically rope, curl and deform when it is stretched or placed under tension. In the same presentation by Kammerer, significant deformation, in the form of roping/twisting, and curling was also observed in the mechanically-cut mesh (MCM) after it had been elongated by 50%, while the TVT mesh that was laser-cut (LCM) suffered some of the same deformation issues, but to a lesser degree.

Indeed, I personally have witnessed the same type of deformation of the mesh material, *i.e.*, curling, roping/twisting, narrowing and fraying when I have been called upon to remove mesh months or years after implantation. It is my opinion that TVT mesh can rope, curl and deform. Deformation of mesh can create the perfect habitat for bacteria leading to severe infections, inflammation and chronic foreign body response and all of the associated adverse events, such as chronic debilitating pain, difficulty urinating, painful sex, erosions, needing mesh

removal (including multiple surgeries), and urinary incontinence. Deformation of mesh by tensioning can also make the pores of the already small-pore TVT mesh even smaller, creating a higher probability and exacerbation of the adverse outcomes discussed above.²³

2. Laser Cut Mesh Is Stiffer and Less Elastic

The laser cutting technique was developed presumably in an effort to address the chronic problems of particle loss, fraying, sharp edges and other issues inherent in mechanically-cut mesh. However, laser cut products have their own problems.

Ethicon's own testing revealed that laser cutting the mesh caused it to behave differently than mechanically-cut mesh, particularly with regard to its stiffness and elasticity. The studies showed that laser-cut mesh was indeed substantially stiffer and less elastic.²⁴ Because of its relative lack of elasticity, it is more difficult to achieve proper tensioning with the stiffer laser-cut mesh, and the tendency is to over-tension the product during implantation.²⁵ In addition, stiff mesh can lead to pain, damage to the urethra, and erosions.²⁶

Despite having different mechanical characteristics, Ethicon did not tell doctors via the Instructions for Use for TVT that the laser cut mesh acted differently than the mechanical mesh. Therefore, implanting surgeons would not have known that they needed to tension the TVT sling differently when using a laser cut mesh versus a mechanical mesh. This failure to notify doctors about the differences combined with the fact that the TVT is always implanted via a blind procedure would lead to an increased likelihood that the laser cut TVT would not be implanted tension free, which leads to increased complications as discussed in this report.

²³ Depo. Smith (February 3, 2014) 816:5-15.

²⁴ In an internal memo documenting the results of TM403-477 (Ethicon's standard method for measuring tensile properties of TVT mesh), Ethicon reported that the laser cut mesh was approximately three times stiffer than mechanically-cut mesh after 20% elongation. ETH.MESH.00302181.

²⁵ ETH.MESH.04048515 at 516 (Professor Carl G. Nilsson stated he "will not use Laser-cut mesh!!" as it "does not have the same stretch profile of Mechanical-cut mesh").

²⁶ The Failure Modes and Effect Analysis for laser-cut mesh specifically notes that mesh that is "too stiff" can cause harms such as pain, damage to the urethra, urethral impingement, and damage to the bladder."

E. Cytotoxicity

Cytotoxicity means toxicity to the cells causing cell injury or death.²⁷ In a May 26, 2000, Ethicon Memo titled “Review of biocompatibility on the tension-free vaginal tape (TVT) system for compliance to FDA,”²⁸ the review contains a “Cytotoxicity Risk Assessment for the TVT (Ulmsten) Device” from August 8, 1997.²⁹ The Cytotoxicity Assessment states “there is some evidence to suggest that the PP [polypropylene] mesh from the sterile Ulmsten device may have cytotoxic potential.”³⁰ In addition, ISO Elution testing “resulted in marked cytotoxicity in tests conducted at Ethicon (Scotland).”

It is my opinion based on my professional experience and the research that I have conducted that the adverse outcomes I have seen or researched can be caused and, in some of my patients, were likely caused by the cytotoxicity of the mesh.

F. Polypropylene Is Incompatible with the Vaginal Ecosystem

I have been provided with the Material Safety Data Sheets (“MSDS”) for the polypropylene used in the Prolene mesh for Ethicon’s TVT devices. I have also reviewed a number of other MSDS’s for other similar products. For a number of reasons discussed below, the MSDSs of Phillips Sumika and Chevron Corporation specifically warned that the polypropylene material should never be permanently implanted in the human body.

According to the MSDS for the polypropylene resin used in the Prolene for the TVT devices, the polypropylene is incompatible with “strong oxidizers” such as “peroxides.” Peroxides, particularly hydrogen peroxide, are a critical part of maintaining the vaginal ecosystem. As early as 1987, Ethicon scientists concluded that Prolene was susceptible to

²⁷ Robinson Depo. (September 11, 2013) 1091:11-21.

²⁸ ETH.MESH.06852118 at 2118-2129 (5/26/2000 Biocompatibility Review).

²⁹ ETH.MESH.06852120 (8/8/1997 Cytotoxicity Risk Assessment).

³⁰ *Id.* and Robinson Depo. (September 11, 2013) 1098:23-1099:9.

oxidation which led to degradation of the mesh in vivo. Hence, according to the Prolene MSDS, the polypropylene is incompatible for use in the vagina.

I have also reviewed MSDSs for the polypropylene resin used in other pelvic floor meshes. These MSDSs similarly warn about the incompatibility of the polypropylene with peroxides and discuss how such interactions could lead to degradation of the polypropylene product, such as mesh when exposed to peroxides. Some expressly state that the product should not be used for permanent implantation in the human body.

In my opinion, this information would be important to a treating physician when making the decision whether or not to use a TVT device and also when treating a woman who has suffered from complications from a TVT device. For example, when explanting mesh, it often is very difficult to remove all of the mesh as often it has frayed, degraded or some portions have been fully in-grown. However, understanding that the mesh is incompatible with the very space where it is implanted and that leaving any mesh in place might exacerbate or even continue to cause the initial problem might militate in favor of taking a more aggressive approach to removal.

In my review of the documents provided to me for this report, it is clear that Ethicon never informed physicians of this incompatibility and the potential adverse outcomes that could arise. It is also clear from the depositions I reviewed that Ethicon failed to test whether the polypropylene used in the TVT devices was incompatible with the peroxides and other vaginal chemistry and the potential adverse effects that could result.

In addition to these undisclosed risks of incompatibility, the MSDSs I have reviewed expressly discuss a risk of cancer associated with the polypropylene. According to Ethicon employee depositions I have reviewed, Ethicon reproduced this cancer risk in animal studies.

V. THE TVT INSTRUCTIONS FOR USE ("IFU") IS INADEQUATE

In my opinion based on my professional experience, the instructions for use ("IFU") plays an important role in the informed consent process because it provides information for doctors to learn about the risks and benefits associated with a medical implant, such as the TVT. It also provides insights a manufacturer has gained from the worldwide experience with the use of the product, including how to address unique patient attributes and deal with typical complications that may be seen with the device. In my experience, physicians rely upon the device manufacturers to accurately and truthfully describe the known risks and complications associated with the device to allow them to make informed treatment decisions and to allow them to properly consent their patients. In addition, physicians rely upon the IFU to help treat patients who have presented with complications from the device. During the course of my career, I have regularly reviewed IFUs for medical products, including IFUs for mesh slings to treat stress urinary incontinence such as the TVT.

When a patient undergoes a surgical procedure, the surgeon first discusses the risks and benefits with the patient so that the patient may make an informed decision to undergo the procedure. This process is called an informed consent. For a general pelvic surgery, the basic hospital informed consent would cover risks common surgical risks, such as damage to the pelvic structures (GI/GU/vessels/nerves), hemorrhage, infection, urinary incontinence, retention, dyspareunia and recurrent prolapse. If a device is to be used, the surgeon would then rely upon information provided by the manufacturer in the IFU to learn about the warnings specific to that product.

From my extensive experience practicing in medicine and gynecology, talking with other doctors in my field, and speaking at and attending medical conferences, many of the doctors who implanted these products were not aware of many of the risks or their frequency or severity, as

discussed above. The TVT IFU is inadequate because it omits and understates the serious complications discussed above. It also fails to properly inform a physician how to treat a patient who has presented with the above complications. My opinion is further supported by my review of internal Ethicon documents, including statements by Ethicon employees such as Meng Chen and Dr. Aaron Kirkemo.³¹

A. The IFU Omits Many of the Significant Complications

Many of the risks identified in the previous sections are not included in the TVT IFU, such as:

1. TVT was capable of causing chronic, permanent debilitating pain;
2. TVT could cause lifelong risk of erosions;
3. Erosions can be severe, untreatable and incurable;
4. Complications from TVT could cause the patient to need lifelong surgeries to treat mesh erosions and degradation;
5. Serious and chronic inflammation could occur with the use of TVT, and that this complication was not slight or transient;
6. TVT was capable of causing permanent dyspareunia;
7. Eroded mesh posed an injury risk to the woman's partner;
8. TVT mesh was capable of causing Urinary problems, including: Urethral injury, Voiding dysfunction, De novo detrusor instability or urgency, Urinary retention/obstruction, Urinary retention (temporary or permanent), Urinary tract infection, Dysuria, Hematuria, and Worsening or recurrence of incontinence;
9. Mesh was capable of causing permanent nerve injury;
10. Mesh pores could collapse under strain and cause unwanted fibrotic bridging, which was capable of causing painful scarring, permanent tissue damage, nerve pain and entrapment, dyspareunia, urinary and defecatory problems, and chronic debilitating pain;
11. The polypropylene TVT mesh was capable of degrading;
12. TVT mesh was cytotoxic;
13. TVT could cause toxic shock syndrome;
14. TVT can cause serious, difficult to treat infections, de novo urinary tract infections, inflammation and that the changes to the vaginal ecosystem from these imbalances can potentiate mesh degradation and chronic foreign body reaction;
15. Particle loss was a known problem and that it contributed to further unwanted foreign body reaction;
16. Ethicon possessed evidence that the risk of vaginal scarring was greater than disclosed in its IFU;
17. Use of TVT could cause narrowing of the vaginal wall;

³¹ ETH.MESH.04092868; ETH.MESH.0494863.

18. Ethicon did not have any procedure or Professional Education program to teach doctors how to properly remove TVT mesh slings when known complications occurred;
19. Manufacturers of polypropylene resin stated that it should not be used for medical purposes or permanent implantation in the human body;
20. That the polypropylene resin used for the mesh in the TVT induced sarcomas at the site of implantation.

B. The IFU Understates the Severity and Frequency of the Complications

The IFU also uses language that understates the known risks listed in the IFU, such as “transitory” or “rare” or “typical”. This language understates the frequency of the adverse outcomes, the severity of those complications, and the duration of those complications. In my experience and my review of the medical literature, and as admitted in numerous Ethicon documents described above, the complications from TVT are far from transitory, and that the complications and injuries suffered by patients are often long term and permanent.

C. The IFU Does Not Adequately Discuss Methods to Treat Complications, Including the Safest Methods to Remove a TVT

The TVT IFU did not inform physicians about techniques to treat complications from TVT mesh. From my experience, it is important for doctors to know what to look for and where to look when performing a revision surgery. Ethicon has more information from its worldwide database and experience from sales representatives than anyone else regarding the most effective and safest methods to treat complications. Further, Ethicon did not provide information in the IFU about the significant dissection associated with surgery to explant the TVT mesh. Ethicon did not warn doctors that it is almost impossible to fully remove all of the mesh once it has been integrated into the tissue or degraded. Finally, Ethicon did not warn in the IFU that revision surgery further increases scar tissue, leading to increased complications such as pain, disfigurement, and dyspareunia.

D. The IFU Does Not Address Special Patient Populations

The TVT IFUs offer no guidance for physicians on use of the TVT mesh products in special patient populations. For example, studies have shown the TVT device is not as effective and can cause more complications in women who are obese, diabetic, smokers, older women, women with pre-existing or who might develop pelvic pain or myalgias and younger athletic women. Further, research has shown that there are anatomical differences between individuals and between different ethnicities generally. Even with highly skilled surgeons, it is impossible to fully predict and account for anatomical differences when implanting the TVT mesh via the blind passage. Yet, the IFU does not inform physicians (who in turn cannot inform patients) of these known risks.

E. Bi-Directional Properties of the Mesh

Ethicon states in the TVT Instructions for Use (“IFU”) that Prolene mesh is knitted by a process “which interlinks each fiber junction and which provides for elasticity in both directions. This bi-directional elastic property allows adaptation to various stresses encountered in the body.”³² Ethicon has never performed a study to determine what bi-directional forces are present in the pelvic region, or tested how its TVT product is able to meet those requirements. Instead, and as discussed above, the implanted mesh creates a chronic foreign body reaction, which can lead to the formation of a rigid scar plate and contraction of the mesh implant. As such, the mesh is not capable of adapting to various, bi-directional stresses in the body. In my opinion, this information would be important to a treating physician when making the decision whether or not to use a TVT device and also when treating a woman who has suffered from complications from a TVT device.

³² ETH.MESH.00353639, ETH.MESH.00015699 –00015706; ETH.MESH.00013506; ETH.MESH.00922443-00922445; ETH-00938; Walji Deposition p471-472; Robinson Deposition 3-14, p683-684; Kirkemo Deposition 4-18, p246-247, Ciarrocca Deposition 3-29, p264

VI. THE SIGNIFICANT RISKS OUTWEIGH THE POTENTIAL BENEFIT

In my experience and professional opinion, the benefits of Ethicon's TVT product are outweighed by the significant risks that the products pose to the health of the patients in the long term. As discussed above, there are numerous serious complications associated with implanting the TVT sling for treatment of stress urinary incontinence, including death, permanent disfigurement, and chronic pain. Based on my surgical experience in removing mesh from women and years of experience reviewing mesh related complications, I have reached the opinion that polypropylene mesh has harmful effects for women when permanently implanted in the pelvic region. I have seen how the polypropylene mesh reacts with major organs in the pelvic region. It is my opinion that polypropylene mesh permanently implanted in the pelvic region has a propensity to shrink, contract, erode, degrade, sustain particle loss and fraying, and cause a chronic foreign body reaction, fibrotic bridging and scar plating. All of these propensities result in harmful complications for the patient.


Studies have shown that the TVT device is no more efficacious at treating stress urinary incontinence than other procedures that do not involve mesh. Multiple alternative therapies and procedures (surgical and non-surgical) are available for the treatment of SUI, including but not limited to Burch procedures (which use the patient's own ligaments to support the prolapse), removable pessary devices, urinary seals, urethral inserts, bulking agent injections, medications and pelvic muscle exercises (or "Kegel"). When weighing the risks and benefits with the TVT product, it is important to note that stress urinary incontinence is not a life threatening condition and does not cause chronic and debilitating pain.

In further support of my opinion that the risks outweigh the benefits, it is commonly accepted that the true rate of risks is likely higher than what published in the scientific literature. Research has shown that adverse events are commonly underreported, including complications

with mesh slings for treatment of stress urinary incontinence. Additionally, many of the safety and efficacy studies for these products were performed by persons with a financial interest in selling these products. Accordingly, the true rate of complications is likely understated and the actual rate of success is likely overstated, both of which further support my opinion that the risks are outweighed by the benefits.

I reserve the right to update my opinions if additional materials become available.

February 1, 2016



Michael Thomas Margolis, M.D.

VII. EXHIBITS

My current curriculum vitae is attached hereto as Exhibit "A"

All exhibits that will be used to support my findings and opinions or documents that I have reviewed are referred to herein or in Exhibit "B"

VIII. RECENT TESTIMONY

In the previous four years, I have testified, by deposition or in trial, in the following cases:

- Coleen Perry v. Luu, et al.
- Martha Salazar v. Lopez, et al.
- Linda Batiste v. Johnson & Johnson and Ethicon, Inc.
- Elizabeth Ayerdis v. Hawaii Permanente Medical Group
- Carpenter v. Hardesty, et al; Superior Court of the State of California, San Bernadino County
- Sabrina Gaines v. Kendal Freeman, et al.
- Gross v. Gynecare, New Jersey Superior Court, Atlantic County Division
- Harrison v. Eberts
- Lorie Koop v. George Stankevych
- Tracey Patane v. Ardent Health Services, et al.

- Pamela Russell v. Neil Harrison, et al.
- Rizzo, et al. v. C.R. Bard, Inc., United States District Court, Northern District of Georgia
- Scorpio v. Noone
- Waddoups v. Barry Noorda, et al., United States District Court, District of Utah
- Nancy & Gary Fleming v. Boston Scientific
- Mildred Blankenship v. Boston Scientific
- Penny Barton v. Boston Scientific
- Catherine Pickle v. Boston Scientific
- Esbarda Chapa v. Boston Scientific
- Gwendolyn Gravitt v. Boston Scientific
- Hilda Escalante v. Bard
- Glory Lewis v. Bard
- Rebecca George –2:12-cv-03585
- Gilbert v C.R. Bard, Inc.: Case No.: 2:14-cv-00404
- Sherrer v Boston Scientific Corporation, et al: Case No.: 1216-cv27879
- Carlino v Ethicon (Ongoing in Philadelphia right now)